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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/599,913	10/23/2006	Hyae Gyeong Cheon	DE1700PCT	6550

1109 7590 11/19/2008

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EXAMINER	
BAEK, BONG-SOOK	
ART UNIT	PAPER NUMBER
1614	
MAIL DATE	DELIVERY MODE
11/19/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/599,913	CHEON ET AL.	
	Examiner	Art Unit	
	BONG-SOOK BAEK	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 October 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 4-9* is/are pending in the application.

4a) Of the above claim(s) *5-7* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 4, and 8-9* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of claims

The amendment filed on October 3, 2008 is acknowledged. Claims 2-3 have been canceled and claims 5-7 have been withdrawn. Claims 1, 4, and 8-9 are under examination in the instant office action.

Applicants' arguments, filed on 10/3/2008, have been fully considered but they are not deemed to be persuasive. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application. Responses are limited to Applicants' arguments relevant to either reiterated or newly applied rejections.

Rejections maintained

The rejection of the claims 1 and 8-9 under 35 USC 112, first paragraph is maintained for reasons of record and the following.

Applicants stated that they have amended claim 1 to limit the scope of formula (I) in conjuction with Table I of the specification. However, the amendments are not fully responsive for enablement requirements with regard to use aspect of the specification. As stated in the previous action mailed on 7/3/2008, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims, especially claims 8-9. The instant invention is

directed to compounds which allegedly have modulating peroxisome proliferator-activated receptor (PPARs) and can be used for the treatment of various disorders such as diabetes, obesity, atherosclerosis, hyperlipidemia, hypertension, osteoporosis, liver cirrhosis, asthma, and cancer. PPARs are a group of nuclear receptor proteins that function as transcription factors regulating the expression of genes and play essential roles in the regulation of cellular differentiation, development, and metabolism (carbohydrate, lipid, and protein) of higher organisms. As stated in the previous action, there are three types of PPARs, alpha, gamma, and delta, which are expressed in different levels in different tissues and have different physiological effects (Berger *et al.*, Annu Rev Med, vol. 53, p409-435, 2002). Therefore, based on which subtype of PPARs is modulated by the claimed compound, different outcome would be resulted in. However, the disclosure is limited to the results of receptor binding activity of limited number of compounds for only peroxisome proliferator-activated receptor-γ (PPAR-γ) and a biological activity for only elected species. The pharmaceutical art is unpredictable and target compounds need to be individually assessed for viability. Extremely broad generalizations as found in the instant claims are in contradiction with the basis of quantitative structure-activity-relationship (QSAR). In addition, in spite of the narrow structural characteristics (see above) of the disclosed compounds, the biological activity seems to vary widely. Thus it is unpredictable what specific embodiment of the billion possibilities of the instant claims would have the desired biological properties.

New ground of rejections necessitated by Applicant's amendment

Claim Rejections - 35 USC § 112, 1st paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1 and 8-9 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 1 recites the variables R^2 is CN, CO_2R^a or $CONR^j$. When R^2 is $CONR^j$, one more valency is available for nitrogen atom to make a bond. The instant claim as amended recites no limitation or definition for a substituent for that valency, which is interpreted as any substituent can be attached to the nitrogen atom, thus it encompasses a broader scope than the original claim and the specification. Therefore, it is considered as new matter.

Claims 8-9 are rejected because they are dependent from claims 1, thus incorporates its limitation.

Claim Rejections - 35 USC § 112, 2nd paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1 and 8-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In the instant case, claim 1 recites the variables R^i is C_{1-6} alkyl. R^i

variable is currently not part of the claimed invention and one of ordinary skill in the art would not know what they represent. In addition, claim 1 recites the variables R^2 is CN, CO_2R^a or $CONR^j$. When R^2 is $CONR^j$, one more valency is available for nitrogen atom to make a bond. The instant claim as amended recites no limitation or definition for a substituent for that valency, which is interpreted as any substituent can be attached to the nitrogen atom. Thus, one of ordinary skill in the art would not know the metes and bounds of the patent protection desired.

Claims 8-9 are rejected because they are dependent from claims 1, thus incorporates its limitation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

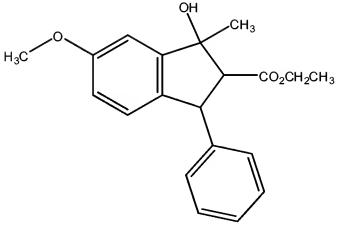
> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. § 103(c) and potential 35 U.S.C. § 102(e), (f) or (g) prior art under 35 U.S.C. § 103(a).

Claims 1, 4 and 8-9 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rayabarapu *et al.* in view of US patent 3,642.785 (patented on 2/15/1972).

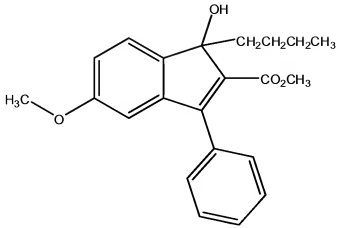
Applicants argue that Rayabarapu *et al.* discloses an indenol derivative whose 5- position is substituted by methoxy group and 6-position is unsubstituted, unlike formula(I) of the present invention as amended and Rayabarapu *et al.* are quite clear that the compounds disclosed in their article are "completely regioselective", thus prior art teaches away from compounds that vary from those listed in its Tables in the pages 9-10 of the response filed on 10/3/2008. It further argues that Rayabarapu does not disclose the pharmaceutical use of an indene derivative. The argument has been fully considered but is not found to be persuasive as for reasons of record and the following.

The following compound is recited in the instant claim 4.



1-hydroxy-6-methoxy-1-methyl-3-phenyl-1H-indane-2-carboxylic acid ethyl ester

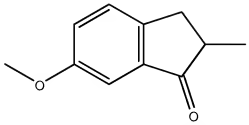
Rayabarapu *et al.* teach the following indenol compound (p6727, table 2, entry 16) as stated in the previous action mailed on 7/3/2008.



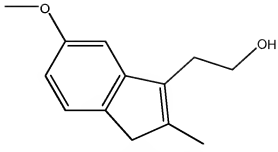
The reference mentioned that the carbocyclization reactions are completely regioselective giving only the Michael-type addition product (p6727, right column, 2nd paragraph), which is directed to the positions 2 and 3 of the indene ring, but not relevant to the positions 5 and 6. Thus, the prior art does not teach away from the instantly claimed compounds.

The difference between the instant compound as amended and that of the prior art is that the instant compound has methyl group instead of butyl in the position 1 of indene ring; ethyl ester rather than methyl ester at the position 2; and has a methoxy group at the position 6 instead of the position 5.

US patent 3,642,785 teaches compounds of the following structure, which show modification of the position of methoxy group from the position 5 to the position 6 in the similar core structure to that of the instant compounds while retaining the same activity (example 3 and example 6):

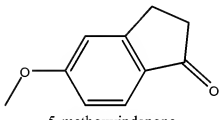


2-methyl-6-methoxyindanone

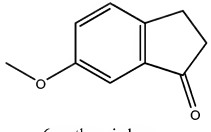


2-methyl-5-methoxy-3-indenethanol

It further teaches that many indanones such as the following 5-methoxyindanone and 6-methoxyindanone are known in the literature and are readily available as intermediates for the synthesis (column 10, lines 9-30):



5-methoxyindanone



6-methoxyindanone

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to modify the compound taught by Rayabarapu *et al.* to arrive at the instantly claimed compound because of the following reasons: First, US patent 3,642,785 suggests that change in the position of methoxy group at the similar core structure would be possible while retaining the same activity and teaches that positional isomers such as 5-methoxyindanone and 6-methoxyindanone are readily available for synthesis. Also, it is routine experimentation to substitute a methyl group with longer alkyl group such as $C_{2\text{-}5}$ alkyl group or vice versa in the field of medicinal chemistry. To those skilled in the art of medicinal chemistry, one homologue is not such an advance over adjacent member of series as requires invention

because chemists knowing properties of one member of series would in general know what to expect in adjacent members. *In re Henze*, 85 USPQ 261 (1950). In addition, one skilled in the art at the time the invention was made would be obvious to be motivated to make analogs of Rayabarapu *et al.* to arrive at other biologically active indenol compounds with reasonable expectation of success since Rayabarapu *et al.* teach indenol moiety is an important and central structural unit present in various biologically active compounds (p6726, left column 1st paragraph) as stated in the previous action.

With regard to the pharmaceutical use of indene derivatives as recited in the instant claims 8-9, an intended use does not have a patentable weight since the instant invention is directed to a compound (product). In accordance with the patent statutes, an article or composition of matter, in order to patentable, must not only be useful and involve invention, but must also be new. If there is no novelty in an article or composition itself, then a patent cannot be properly granted on the article or composition, regardless of the use for which it is intended. The difficulty is not that there can never be invention in discovering a new process involving the use of an old article, but that the statutes make no provision for patenting of an article or composition which is not, in and of itself, new.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BONG-SOOK BAEK whose telephone number is 571-270-5863. The examiner can normally be reached 8:00-5:00 Monday-Thursday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel can be reached on 571-272-0718. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Brian-Yong S Kwon/
Primary Examiner, Art Unit 1614
Bbs

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